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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,248	03/29/2000	David A. Cheresh	TSRI-651.3	6166

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/08/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/538,248	Cheresh et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on Dec 17, 2001

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) 1-31 is/are pending in the applica

4a) Of the above, claim(s) 5-15 and 21-31 is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) 1-4 and 16-20 is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6

18) [ ] Interview Summary (PTO-413) Paper No(s) _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other

Applicant's election with traverse of Group I, Claims 1-4 and 16-20 in Paper No. 9 is acknowledged. After further consideration of applicants arguments and the claims the previous restriction is hereby modified to be a restriction and election of species requirement as detailed below.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9, and 16-25 drawn to drawn to methods of ameliorating tissue damage from vascular leakage or edema by treating with compositions of a Src family tyrosine kinase inhibitor and pharmaceutical products therefor, classified in class 514, subclasses 258, 450, 183, and 789 or class 424, subclass 94.5.

II. Claims 10-15 and 26-31, drawn to drawn to methods of ameliorating tissue damage from vascular leakage or edema by treating with compositions of nucleic acids encoding a Src family tyrosine kinase inhibitor protein and pharmaceutical products therefor, classified in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are independent as they comprise distinct chemical products with chemically different and

unrelated structures and distinct functions and the methods each comprise different steps and utilize these different products.

This application contains claims directed to the following patentably distinct species of the invention of Group I: a) pyrazolopyrimidines PP1 and PP2, b) PD173955, c) AGL1872, d) PD162531, e) Radicicol R2146, f) geldanamycin, g) inactive Src proteins, h) inactive Yes proteins, and i) CSK protein. Each of these Src family kinase inhibitors are structurally distinct with no common structural features and would require separate literature searches.

If applicants elect Group I above, applicant is further required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-3, and 16-19 are generic.

This application contains claims directed to the following patentably distinct species of the invention of Group II: a) nucleic acids encoding inactive Src proteins, b) nucleic acids encoding inactive Yes proteins, and c) nucleic acids encoding CSK protein. Each of these nucleic acids are structurally distinct with no common structural features and would require separate literature searches.

If applicants elect Group II above, applicant is further required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 10-13, and 26 are generic.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

As each of the groups previously presented in the earlier restriction requirement correspond to one of the current groups and one of the species of the current restriction and election of species, applicants election of restriction group I is taken as a provisional election of Group I and the species of pyrazolopyrimidines PP1 and PP2 for examination on the merits.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the

inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claims 5-15 and 21-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant traversed the restriction (election) requirement in Paper No. 9, however, the traverse is considered moot in view of the recharacterization of the previous restriction as a restriction and election of species. If applicants disagree they may further traverse in response to the current Office Action.

Claims 3-4 and 19-20 are objected to because of the following informalities: abbreviations (such as "PP1 or PP2") should not be used in the claims without reciting the full terminology for which they are used unless they are common within the art. It is noted that in this instance the abbreviations are particularly confusing as the same abbreviations are used in the art to mean protein phosphatase 1 and protein phosphatase 2. Appropriate correction is required.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of van Bruggen et al., Aiello et al. (US Patent 6,284,751) or Jirousek et al. (US Patent 6,093,740) in view of Munshi et al.

van Bruggen et al. teach methods of treating edema formation in mouse brain by administering an inhibitor of VEGF signaling (a truncated Flt-1 receptor fused to a Fc-IgG). van Bruggen et al. do not teach treating edema with a Src family tyrosine kinase inhibitor such as PP1.

Aiello et al. teach methods of inhibiting vascular permeability, in particular treating pulmonary edema formation, by administering an inhibitor of VEGF signaling (a selective PKC inhibitor). Aiello et al. specifically teach that there is a need

in the art to develop new therapeutic agents targeted at VEGF function (see column 2, lines 23-26). Aiello et al. do not teach treating edema with a Src family tyrosine kinase inhibitor such as PP1.

Jirousek et al. teach methods of inhibiting vascular permeability, in particular treating dermal edema formation, by administering an inhibitor of VEGF signaling (a selective PKC inhibitor). Jirousek et al. specifically teach that there is a need in the art to develop new therapeutic agents for skin lesion treatment, especially therapeutic agents targeted at VEGF stimulated vascular permeability (see column 2, lines 4-8). Jirousek et al. do not teach treating edema with a Src family tyrosine kinase inhibitor such as PP1.

Munshi et al. teach that the pyrazolopyrimidine PP1 is a selective inhibitor of Src family kinases and inhibits VEGF signaling pathways.

Therefore, it would have been obvious to one of ordinary skill in the art to substitute PP1 for the VEGF inhibitor of van Bruggen et al., Aiello et al., or Jirousek et al. as Munshi et al. teach that PP1 is another inhibitor of VEGF signaling and thus would be expected to have similar therapeutic effects as the VEGF inhibitors of van Bruggen et al., Aiello et al., or Jirousek et al.

Claims 1-4 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of van Bruggen et al., Aiello et al. (US Patent 6,284,751) or Jirousek et al. (US Patent 6,093,740) in view of Hanke et al. and either of He et al. or Cooke et al.

van Bruggen et al., Aiello et al. and Jirousek et al. are discussed above.

He et al. teach that the pyrazolopyrimidine PP2 is a selective inhibitor of Src family kinases and inhibits VEGF signaling pathways.

Cooke et al. teach that the pyrazolopyrimidine PP2 is a selective inhibitor of Src family kinases and inhibits VEGF signaling pathways.

Hanke et al. that the pyrazolopyrimidines PP1 and PP2 are highly structurally related and both act as selective inhibitors of Src family tyrosine kinases.

Therefore, it would have been obvious to one of ordinary skill in the art to substitute PP2 or PP1 for the VEGF inhibitor of van Bruggen et al., Aiello et al., or Jirousek et al. as He et al. and Cooke et al. teach that PP2 is an inhibitor of VEGF signaling and Hanke et al. teach that PP1 has the same functional effect as PP2 and thus both PP1 and PP2 would be expected to have

similar therapeutic effects as the VEGF inhibitors of van Bruggen et al., Aiello et al., or Jirousek et al.

Claims 1-4 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of van Bruggen et al., Aiello et al. (US Patent 6,284,751) or Jirousek et al. (US Patent 6,093,740) in view of Hanke et al. and Eliceiri et al. (1998).

van Bruggen et al., Aiello et al., Jirousek et al. and Hanke et al. are discussed above.

Eliceiri et al. teach that Src kinase is required for VEGF signaling pathways.

Therefore, it would have been obvious to one of ordinary skill in the art to substitute PP1 or PP2 for the VEGF inhibitor of van Bruggen et al., Aiello et al., or Jirousek et al. as Eliceiri et al. teach that Src Kinase activity is required for VEGF signaling pathways and Hanke et al. teach that PP1 and PP2 inhibit Src kinase activity and thus PP1 and PP2 would be expected to have similar therapeutic effects as the VEGF inhibitors of van Bruggen et al., Aiello et al., or Jirousek et al..

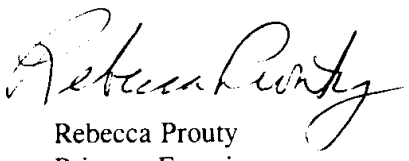
It is noted that several of the cited references were published after the claimed priority dates of the instant application, however, none of the claimed prior applications teach the use of small organic chemical inhibitors of Src family

tyrosine kinases and in particular PP1 or PP2 for treatment of conditions related to vascular leakage or edema and neither PCT/US99/11780 nor provisional application 60/087,220 provide support for treatment of conditions related to vascular leakage or edema as is currently claimed. As such the instant claims have not been granted the benefit of the filing date of the prior applications.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Rebecca Prouty
Primary Examiner
Art Unit 1652